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10/593,567	08/21/2007	Harald Groeger	294227US0X PCT	1637

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EXAMINER	
POPA, ILEANA	
ART UNIT	**PAPER NUMBER**
1633	

NOTIFICATION DATE	DELIVERY MODE
10/28/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/593,567	GROEGER ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 3, and 5 have been amended. Claims 7-16 are new.

Claims 1-16 are pending and under examination.

2. The objection to the oath or declaration is withdrawn in response to applicant's arguments field on 08/17/2010.

The following rejections are withdrawn in response to the claim amendments filed on 08/17/2010:

The rejection of claims 1-6 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 4-7 of U.S. Patent No. 7,217,544, in view of Hong;

The rejection of claims 1-6 under 35 U.S.C. 112, second paragraph, as being indefinite;

The rejection of claims 1-6 under 35 U.S.C. 103(a) as being unpatentable over Galkin et al. (Appl. Environm. Microbiol., 1997, 63: 4651-4656), in view of each Hong (Biotechnol. Bioeng., 1986, 28: 1421-1431), Smith et al. (J. Biol. Chem., 1993, 268: 10746-10753) and Neuhauser et al. (Biotechnol. Bioeng., 1998, 60: 277-282).

Response to Arguments

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as

to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-6 remain and the new claims 7-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5-8 and 10-13 of copending Application No. 12/205,371, in view of Hong (Biotechnol. Bioeng., 1986, 28: 1421-1431). Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets encompass preparing enantiomerically-enriched α-amino acids of Formula (I) by reacting 2-ketocarboxilic acids with an ammonium donor in the presence of a whole cell catalyst comprising a gene encoding a cofactor-dependent amino acid dehydrogenase and a gene encoding an enzyme capable of regenerating the cofactor such as glucose dehydrogenase.

Although the application claims do not recite a fed-batch process, it would have been obvious to one of skill in the art to use such because the art teaches that using fed-batch processes results in higher product yield (see Hong, Abstract, p. 1421, column 1, p. 1430, column 2, p. 1431, column 1, p. 1425, column 2).

Although the application claims recite reacting a ketone with an α-amino acid, an ammonium donor and a reducing agent in the presence of a whole cell catalyst expressing an amino acid transaminase, an amino acid dehydrogenase and an enzyme which reacts with NAD to regenerate NADH (i.e., cofactor), the transaminase catalyses the reaction between the ketone and the α-amino acid to yield the 2-ketocarboxylic acid, which in turn is converted to an enantiomerically-enriched α-amino acid. Thus, the enantiomerically-enriched α-amino acid is obtained from a 2-ketocarboxilic acid in the method recited in the application claims. It is noted that, although the instant claims do not recite that the whole cell catalyst expresses a transaminase, the broad language used in the instant claims does not exclude its presence.

Although the application claims do not specifically recite treating the whole cell catalyst to increase the permeability of the cell membrane, it would have been obvious to one of skill in the art to do such with the purpose of increasing the yields.

Although the instant claims do not recite NADH, such is inherent to the whole cell catalyst, which comprises NADH. With respect to the limitation of a reducing agent such as glucose, the instant specification defines that reaction medium comprises glucose (p. 12, line 20 through p. 13, line 1).

Thus, the instant claims and the application claims are obvious variants.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The applicant argues that the instant rejection should be withdrawn because the instant claims have been amended to recite glucose dehydrogenase. This is not found persuasive because the application claims also recite glucose dehydrogenase.

New Rejections

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-6 remain and the new claims 7-16 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 4-7 of U.S. Patent No. 7,217,544, in view of both Hong and Yamamoto et al. (PGPUB 2002/0064847). Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets encompass preparing enantiomerically-enriched α-amino acids of Formula (I) by reacting 2-ketocarboxilic acids with an ammonium donor in the presence of a whole cell catalyst comprising a gene encoding a cofactor-dependent amino acid dehydrogenase and a gene encoding an enzyme capable of regenerating the cofactor. Although the patent claims do not recite an ammonium donor, the patent specification defines that the reaction medium comprises NH_4Cl (i.e., ammonium donor) (column 11, Example 4). The patent claims recite malate or formate and not glucose dehydrogenase. However, the prior art teaches that malate, formate, and glucose dehydrogenases are equivalent (see Yamamoto et al., p. 4, paragraph 0046). Thus, one of skill in the art would have found it obvious to modify the patent claims by replacing the malate or formate dehydrogenase with glucose dehydrogenase to achieve the predictable result of producing optically active amino acids.

Although the patent claims do not recite a fed-batch process, it would have been obvious to one of skill in the art to use such because the art teaches that using fed-batch processes results in higher product yield (see Hong, Abstract, p. 1421, column 1, p. 1430, column 2, p. 1431, column 1, p. 1425, column 2).

Although the patent claims recite reacting a D-amino acid in the presence of a whole cell catalyst expressing a D-amino acid oxidase, an amino acid dehydrogenase and an enzyme which regenerates NADH (i.e., cofactor), the D-amino acid oxidase catalyses oxidation of the D-amino acid to the corresponding 2-ketocarboxylic acid, which in turn is converted to an enantiomerically-enriched α-amino acid. Thus, the enantiomerically-enriched α-amino acid is obtained from a 2-ketocarboxilic acid in the method recited in the patent claims. It is noted that, although the instant claims do not recite that the whole cell catalyst expresses a D-amino acid oxidase, the broad language used in the instant claims does not exclude its presence.

Although the instant claims do not recite NADH, such is inherent to the whole cell catalyst, which comprises NADH. The instant specification also defines that the amino acid dehydrogenase could be from *Bacillus cereus* (p. 7, lines 10-14) and that the whole cell catalyst could be *E. coli* (p. 9, line 36 through p. 10, line 5).

Thus, the instant claims and the patent claims are obvious variants.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galkin et al. (Appl. Environm. Microbiol., 1997, 63: 4651-4656, of record), in view of

each Yamamoto et al. (PGPUB 2002/0064847), Hong (Biotechnol. Bioeng., 1986, 28: 1421-1431, of record), and Smith et al. (J. Biol. Chem., 1993, 268: 10746-10753, of record).

Galkin et al. teach a batch processing method for obtaining enantiomerically enriched L-α-amino acids, the method comprising reacting corresponding 2-keocarboxylic acids and ammonium formate (i.e., an ammonium donor) in the presence of *E. coli* cells genetically engineered to express a NADH-dependent L-amino acid dehydrogenase (such as leucine, phenylalanine or alanine dehydrogenase) and formate dehydrogenase capable of regenerating NADH, wherein no cofactor is added to the reaction mixture and wherein the stationary concentration of 2-keocarboxylic acids is 0.05 to 0.3 M (claims 1-3, 5, 9, 10, 12, and 16) (Abstract, p. 4651, column 2, p. 4652, column 2 and Fig. 1, p. 4653, columns 1 and 2). Galkin et al. also teach that the bacterial cells could be pretreated such as to increase the permeability of the cell membrane (claims 6 and 13) (p. 4655, column 1, second full paragraph).

Galkin et al. teach formate and not glucose dehydrogenase. However, the prior art teaches that formate and glucose dehydrogenases are equivalent (see Yamamoto et al., p. 4, paragraph 0046). Thus, one of skill in the art would have found it obvious to replace the formate dehydrogenase of Galkin et al. with a glucose dehydrogenase to achieve the predictable result of producing optically active amino acids.

Galkin et al. teach a batch and not a fed-batch process (claims 1, 4, and 11). However, doing such is suggested by the prior art. For example, the prior art teaches that fed-batch is superior to batch processing with respect to the yield of the desired

product because it is able to prevent enzyme inhibition by substrate and/or product; in the fed-batch process, the substrate is fed to the fermentor at a controlled rate such that the substrate concentration is kept constant at a optimal, pre-determined stationary value (see Hong, Abstract, p. 1421, column 1, p. 1430, column 2, p. 1431, column 1, p. 1425, column 2). Furthermore, the prior art teaches that amino acid dehydrogenases are inhibited by substrate (see Smith et al., p. 10746, column 1). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Galkin et al. by substituting their batch process with a fed-batch process with a reasonable expectation of success. One of skill in the art would have been motivated to do such because the art teaches that using fed-batch processes results in better product yields. One of skill in the art would have reasonable expected to be successful in doing such because the art teaches that fed-batch could be successfully used in fermentation processes. With respect to the limitation of a total substrate input of more than 500 mM being metered such that the stationary concentration of 2-keocarboxylic acids is less than 500 mM (claim 1), it would have been obvious to one of skill in the art to optimize the yield by varying the substrate input. With respect to the limitations recited in claims 7, 8, 14, and 15, one of skill in the art would have known that the process could be used to prepare any amino acid.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

The applicant argues that the specification teaches that use of glucose dehydrogenase leads to a conversion of 97%, which is not achieved by Galkin et al. and which is not reasonably predicted from the combined teachings of the cited art. This is not found persuasive. Specifically, the applicant did not provide any evidence that specifically using glucose dehydrogenase results in a higher conversion as opposed to using the other enzymes taught by the art. In fact, it is the use of fed-batch, and not glucose dehydrogenase, which results in high conversion and this is taught by the cited art. Based on the teachings in the prior art, one of skill in the art would have expected to achieve superior amino acids yields.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633